

**Title: ILIOINGUINAL/ILIOHYPOGASTRIC VS. QUADRATUS LUMBORUM NERVE  
BLOCKADE FOR ELECTIVE OPEN INGUINAL HERNIORAPHY**

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**Study Title: Ilioinguinal/Iliohypogastric vs. Quadratus Lumborum Nerve Blockade for Elective Open Inguinal Herniorrhaphy**

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**Background, Rationale and Context**

Open inguinal herniorrhaphy is a common outpatient surgical procedure. Post-operative pain can be a significant hindrance to discharge from the post anesthesia care unit. Pain can be treated with opioid therapy, but the literature supports that these agents are known to create or exacerbate adverse effects and complications, including post-operative nausea and vomiting, hypoxia, and urinary retention. In contrast, analgesia provided by regional anesthesia results in a decreased risk of the aforementioned complications.<sup>1</sup> Because of this, various regional anesthetic techniques have been developed to provide analgesia following open herniorrhaphy. One technique is a combined ilioinguinal and iliohypogastric nerve block (IINB), which has been shown to decrease the initial pain after inguinal herniorrhaphy.<sup>2</sup>

The quadratus lumborum block (QLB) is a newer regional anesthetic technique that we think could be as effective as IINB at providing pain control following open herniorrhaphy. Additionally, because local anesthetic injected during a QLB has the potential to spread cranially into the thoracic paravertebral space following its lumbar deposition it could lead to alleviation of both somatic and visceral pain.<sup>3</sup> This might therefore improve the quality and or duration of analgesia as compared to the IINB. To the best of the author's knowledge there has been no investigation comparing the efficacy, with regards to post-operative pain management, between IINB and QLB.

**Objectives**

This study will seek to investigate the efficacy of two distinct nerve blocks (QLB vs. IINB) with regards to post-operative pain scores with movement following an open inguinal hernia repair. We hypothesize that the QLB will provide equivalent analgesia when compared to the IINB as determined by a comparison of verbal reported pain scores.

**Methods and Measures**

**Design**

- This study will be a double-blinded prospective randomized controlled equivalency trial comparing QLB to IINB.

**Setting**

- The setting for the study will be an academic medical center and all patients recruited will have surgery at Wake Forest Baptist Medical Center.

**Subjects selection criteria**

Patients with a diagnosis of inguinal hernia scheduled for elective unilateral open inguinal hernia repair.

- **Inclusion Criteria**
  - All patient's scheduled for elective unilateral open inguinal hernia repair
- **Exclusion Criteria**

- The anesthesiologist performing the intraoperative anesthetic deems the patient inappropriate for general anesthesia.
  - If the patient uses more than 40mg of Oxycodone equivalents per 24 hours or is on extended release opioid formulations.
  - If there is a contraindication to the performance of a regional block
    - Concomitant anticoagulation use
    - Allergy to local anesthetic
    - Infectious or dermatologic conditions in the area of block placement that would otherwise increase the risk of peripheral nerve blockade
  - Patient refusal
  - Pregnancy
  - Institutionalized individuals
  - Extremes of age: Age > 90 or < 18
  - Non English speaking
- **Sample Size**
    - The study design will compare X and Y for postoperative pain following Z. The trial will compare these two approaches for postoperative pain control under the hypothesis that X will provide equal to Y. Using an 11-point numerical pain scale (0-10), the study will be powered to find that the average numeric pain score on the pain scale (8 hours following block placement) following the two approaches does not differ by more than 2 points. The assumption for this study is that differences of less than 2 numerical points on the pain scale are not clinically significant.<sup>4</sup> Preliminary data from 10 II/IH subjects performed at WFUBMC indicates average pain scores with movement of 6.40 at 8 hours post-op (SD=2.41). Assuming an alpha level of 0.05, we therefore estimated that 26 patients in each group would provide a power of 80%. Allowing for potential drop out, we plan to enroll 30 patients per group (60 total patients) in this study.

### **Interventions and Interactions**

- Patients will be randomized to either receive an IINB or QLB for post-operative analgesia
  - Randomization to either QLB or IINB will occur via block randomization using sealed sequentially numbered opaque envelopes that will correspond to the order with which patients are enrolled.
- Patients will be blinded to their randomization by administration of intravenous sedation (titrated to patient comfort), examination of both block sites with ultrasonography, marking of landmarks for each block, and performance of a skin wheel with 1% lidocaine at each block site prior to performance of the randomized block.
- The QLB will be performed in a lateral position in a manner consistent with the technique described by Børglum.<sup>3</sup>
- The IINB will be performed in a supine position in a manner consistent with the technique described by Willschke<sup>5</sup>, but modified to utilize an in-plane technique rather than an out-of-plane technique for needle to ultrasound probe orientation.
- For both QLB and IINB either a Sonosite linear HFL38x/13-6 MHz or Sonosite curvilinear C60x/5-2 MHz probe will be utilized respectively to visualize the pertinent anatomy as outlined in the citations above as well as to visualize the appropriate deposition of local anesthetic.
- For both QLB and IINB a Pajunk 21g x 100mm Sono Plex Stim Cannula will be utilized for placement of local anesthetic.

- For both QLB and IINB the following local anesthetic mixture will be administered
  - Bupivacaine 0.25%
    - Local anesthetic
  - Epinephrine – 5mcg/cc (1:200,000 concentration)
    - Utilized for vasoconstriction, prolongation of regional block, and as an intravascular marker
  - Clonidine – 1.66mcg/cc
    - Utilized for prolongation of regional block and for improvement in block quality.
  - A total of 25cc of the above local anesthetic mixture will be administered in performance of both the QLB and IINB
- An ultrasound image of the block will be saved for both the QLB and IINB as per our normal practice for billing and documentation. This image should be stored on a secure server as per our usual practice with all ultrasound images.
- Block success will be assessed either prior to proceeding to the OR if time permits, or in the immediate post-operative period. Loss of cold sensation in the immediate vicinity of the incisional site will indicate block success.
- Surgeons will be asked to not infiltrate the incision site with additional local anesthetic.
- All patients will receive preoperative multimodal analgesic medications, per the typical approach at our institution. These include acetaminophen orally (1000mg), celecoxib orally (200mg) and pregabalin orally (150mg) unless contraindicated.
- Patients will undergo general anesthesia for the surgical procedure.
- Intraoperative management of the patient will be at the discretion of the attending anesthesiologist for that particular surgery. However, the intraoperative analgesics will be standardized to minimize the chance of their effect on the primary outcome.
  - Patients will not receive ketamine intravenously.
  - Patients will not receive dexamethasone intravenously.
  - Fentanyl intravenously will be the primary analgesic and patients will not receive longer acting intravenous opioids such as hydromorphone or morphine.
- Patients will receive a diary to be completed over the next 24hrs at specific time intervals to aid in collection of data pertinent to both primary and secondary outcomes.
- Postoperative oral pain medications will be ordered as usual by the surgical team without restrictions.
- Patients will be called at home to collect the data from their diary at 8hrs and 24hrs post block.

### **Outcome Measure(s)**

- Primary Outcome
  - Post-operative verbal pain score assessed on an 11-point (0-10) numeric analog scale at 8 hours following block placement during movement.
- Secondary outcomes
  - Post-operative verbal pain score at 8 hours at rest
  - Post-operative verbal pain scores at 24 hours both at rest and with activity
  - Time to first oral analgesic
  - Time when post-operative pain first noted
  - Total opioids used in 24 hours

- Incidence of opioid related side effects (Nausea, Vomiting, and Itching) at both 8 hours and 24 hours

### **Analytical Plan**

The primary analysis will consist of an equivalency comparison between X and Y in terms of their effect on pain scores. For each individual, pain scores will be compared post-op at 8 hours following block placement with movement. Testing equivalency requires specifying a clinical difference (hereafter labeled as d); if the mean difference in pain scores between blocks can be estimated to fall between  $-d$  and  $+d$ , then the two nerve blockades will be deemed equivalent. Equivalence will be tested using the Two One-Sided Tests (TOST) procedure<sup>6</sup>. Preliminary data from 10 II/IH subjects performed at WFUBMC indicates average pain scores with movement of 6.40 at 8 hours post-op (SD=2.41). Power for the TOST procedure can be estimated as in Julious (see equation 5.17)<sup>7</sup>, which accounts for the uncertainty associated with our estimates of the standard deviation in pain scores. Estimated sample size is based on power of 80% and assumes an alpha level of 0.05.

### **Analytic part:**

We will compare the characteristics of patients randomized to the X and Y using t-tests for continuous variables and Chi-Square tests for categorical variable. Equivalence (in terms of the impact of each block on pain) will be tested using the Two One-Sided Tests (TOST) procedure.<sup>6</sup> If we let  $\mu_{AC}$  denote the average change in pain using the quadratus lumborum block, and  $\mu_{LP}$  using the ilioinguinal/iliohypogastric block, the TOST procedure requires rejecting both of the null hypotheses  $\mu_{AC} - \mu_{LP} > 2$  and  $\mu_{AC} - \mu_{LP} < -2$  in order to declare equivalence

### **Human Subjects Protection**

#### **Subject Recruitment Methods**

Potential study participants will be identified by review of the daily operative schedule, and all patients undergoing open inguinal hernia repair will be identified. Preliminary review of the patient's chart will be performed to identify any exclusion criteria as noted above. Should no exclusion criteria be noted, the patient will be identified as a possible study candidate. The patient will be brought to the Regional Anesthesia work area, where the details of the study will be fully disclosed to the patient and consent to participate will be sought.

#### **Informed Consent**

Signed informed consent will be obtained from each subject. Consent will be obtained by the investigators or study coordinator. The consent process for the study will be carried out in the Regional Anesthesia work area.

#### **Confidentiality and Privacy**

Confidentiality will be protected by collecting only information needed to assess study outcomes, minimizing to the fullest extent possible the collection of any information that could directly identify subjects, and maintaining all study information in a secure manner. To help ensure subject privacy and confidentiality, only a unique study identifier will appear on the data collection form. Any collected patient identifying information corresponding to the unique study identifier will be maintained on a linkage file, store separately from the data. The linkage file will be kept secure, with access limited to designated study personnel. Following data collection subject identifying information will be destroyed (*three years after closure of the study via secured document destruction*), consistent with data validation and study design, producing an anonymous analytical data set. Data access will be limited to study staff. Data and records will be kept locked and secured,

with any computer data password protected. No reference to any individual participant will appear in reports, presentations, or publications that may arise from the study.

#### **Data and Safety Monitoring**

The principal investigator will be responsible for the overall monitoring of the data and safety of study participants. The principal investigator will be assisted by other members of the study staff.

#### **Reporting of Unanticipated Problems, Adverse Events or Deviations**

Any unanticipated problems, serious and unexpected adverse events, deviations or protocol changes will be promptly reported by the principal investigator or designated member of the research team to the IRB and sponsor or appropriate government agency if appropriate.

#### **References**

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6. Schuirmann DJ. A Comparison of the Two One-Sided Tests Procedure and the Power Approach for Assessing the Equivalence of Average Bioavailability. *J of Pharamcokinetics and Biopharmaceutics* 1987; 15(6): 657-680.
7. Julious SA. Sample Sizes for Clinical Trials. Chapman and Hall/CRC, Boca Raton, FL, 2010.

#### **Appendix**

1. Data collection form
2. Patient diary
3. Consent form
4. Other Appendix items as appropriate